

REMARKS

In response to the Office Action mailed June 2, 2006, favorable reconsideration is respectfully requested. Claims 19, 61, and 63-64 are currently under examination. By the above amendment, claim 64 has been canceled. The above amendment is made for purposes of advancing prosecution and without prejudice to prosecution of any subject matter removed or modified by this amendment in a related divisional, continuation or continuation-in-part application. Applicants acknowledge and thank the Examiner for withdrawal of the outstanding rejection of claims 19, 22, 61 and 63 under 35 U.S.C. § 103 over Billing-Mendel *et al.*, in view of Hauser *et al.* and Ladd *et al.*

Claims 61, 19, 22, and 63 now stand newly rejected under 35 U.S.C. § 103(a) as being obvious over Momin *et al.* (U.S. Patent No. 6,146,632), Billing-Mendel *et al.* (U.S. Patent No. 6,130,043), and Apostolopoulos *et al.* (Vaccine, 14(9):930-938, 1996).

The Examiner asserts that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the immunogenic composition of Momin *et al.* with the polypeptide of Billing-Mendel *et al.* and administer the immunogenic composition to prostate cancer patients for inducing a Th1-type immune response. According to the Examiner, one of ordinary skill in the art would have been motivated and had a reasonable expectation of success to have produced an immunogenic composition comprising the Th1-inducing immunostimulant composition of Momin *et al.* and the prostate polypeptide of Billing-Mendel *et al.*, because Momin *et al.* teaches compositions comprising a tumor antigen adjuvanted by MPL and QS21, which are preferential stimulators of a Th1 response, Billing-Mendel *et al.* teaches the polypeptide of SEQ ID NO: 36 expressed in prostate cancer, and Apostolopoulos *et al.* teaches that induction of a cellular immune response results in tumor protection.

Applicants respectfully traverse.

Momin *et al.* teaches adjuvant compositions comprising MPL and QS21, and their use for preferential stimulation of IgG2a production and a Th1 cell response. Momin *et al.* also teaches generally that the adjuvant compositions can be used in conjunction with tumor antigens. However, Momin *et al.* certainly does not teach or suggest modifying the described adjuvant

compositions with a polypeptide bearing any structural relationship to SEQ ID NO: 113, much less a polypeptide selected so as to minimally comprise the specific residues 367-375 of SEQ ID NO: 113, as claimed by Applicants.

Billing-Mendel *et al.* teaches a polypeptide of 242 amino acids (SEQ ID NO. 36) expressed in prostate cancer tissue, which shares identity with a portion of the instantly claimed SEQ ID NO. 113. Billing-Mendel *et al.* describes that the polypeptide is a prostate cancer diagnostic marker, and that the polypeptide is used to generate antibodies. However, Billing-Mendel *et al.* does not describe that the polypeptide is to be used in methods for stimulating Th1 cellular immune responses. In fact, the only immune responses disclosed to be of interest to Billing-Mendel *et al.* for the described polypeptide are humoral-based immune responses for producing diagnostic antibodies. In this respect, Billing-Mendel *et al.* teaches away from a need or desirability for making compositions that contain the described polypeptide and that also preferentially stimulate a Th1 type cellular immune response, as claimed by Applicants.

Apostolopoulos *et al.* teaches that induction of a Muc-1 specific humoral immune response (Th2 response) gave poor tumor protection accompanied by little cellular immunity; however, when a Muc-1 specific cellular immune response (Th1 response) was induced, this resulted in significant tumor protection, cytotoxic T lymphocytes, and little antibody production. However, Apostolopoulos *et al.* does not teach or suggest a composition comprising a polypeptide bearing any structural relationship to the polypeptide described by Billing-Mendel *et al.* (or Applicants' SEQ ID NO: 113), or offer any reasonable rationale as to why a skilled artisan would be motivated to modify such a polypeptide to enhance cellular immunity.

The skilled reviewer of Momin *et al.*, would not seek to modify the immunogenic compositions described by Momin *et al.* with the polypeptide of Billing-Mendel *et al.* and administer the immunogenic composition to prostate cancer patients for inducing a Th1-type immune response, as alleged by the Examiner. Momin *et al.* describes an adjuvant system for preferentially inducing a cellular immune response. In this respect, why would the skilled individual, upon review of Momin *et al.*, seek to modify the immunogenic composition of Momin *et al.* with the polypeptide of Billing-Mendel *et al.* and administer the immunogenic composition to prostate cancer patients for inducing a Th1-type immune response, when Billing-

Mendel *et al.* does not teach or suggest that their identified polypeptide is a T-cell antigen, does not describe the T-cell epitope corresponding to amino acid residues 367-375 of SEQ ID NO: 113, as claimed by Applicants, and nowhere describes that the polypeptide is to be administered to a patient for purposes of stimulating a cellular immune response?

The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990). Further, the teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

The Examiner's position, and the motivation to combine Momin *et al.* with one or both of Billing-Mendel *et al.* and/or Apostolopoulos *et al.*, is predicated on the position that Billing-Mendel *et al.* in some way discloses that their identified polypeptide is a human T-cell immunogen that is to be administered to a patient for eliciting a Th1 cellular immune response. Billing-Mendel *et al.* simply does not teach this. This element of the claimed invention can only be found in Applicants' disclosure, not in the prior art. To the extent that Billing-Mendel has any concern with immune responses, it is with humoral immune responses for generating diagnostic antibodies, not with cellular immune responses for stimulating T cells. Absent this teaching by Billing Mendel *et al.*, the skilled reviewer of Momin *et al.* would not find motivation to use a polypeptide of Billing-Mendel *et al.* in the adjuvant compositions described by Momin *et al.*, but instead would seek T-cell antigens in order that the cellular immune response to the antigens might be improved using the adjuvant compositions of Momin *et al.*

Similarly, the skilled reviewer of Billing-Mendel *et al.*, having interest in the diagnostic markers described therein, would not be motivated to turn to Momin *et al.*, Apostolopoulos *et al.*, or any other reference that may describe methods for preferentially stimulating cellular immune responses, when Billing-Mendel *et al.* is concerned solely with humoral immune responses. In this respect, the disclosure of Billing-Mendel *et al.* simply does not support any motivation or desirability of modifying the polypeptide of Billing-Mendel *et al.* for purposes of improving cellular immune responses. This motivation and desirability is also

lacking in the disclosures of Momin *et al.* and Apostolopoulos *et al.* Rather, the motivation and desirability for modifying a polypeptide of Billing-Mendel *et al.* in order to improve the ability of the polypeptide to elicit cellular immune responses is provided only by Applicants' discovery of SEQ ID NO: 113 as an effective human T-cell antigen, and the further identification of the T-cell epitope corresponding to residues 367-375 of SEQ ID NO: 113, as claimed.

Applicants thus submit that the Examiner has improperly attempted to rely upon hindsight reconstruction of elements described in the prior art in an attempt to arrive at the specific invention claimed by Applicants, and in doing so has failed to establish any reasonable rationale or motivation for combining the elements of the cited references in a manner that would lead with any reasonable expectation of success to Applicants' invention.

The Examiner's rejection of claims 64-65 under 35 U.S.C. § 103(a) as being allegedly unpatentable over Billing-Mendel *et al.* in view of Mincheff *et al.* and Apostolopoulos *et al.* is moot in view of Applicants' deletion of these claims.

Applicants respectfully submit that all of the claims remaining in the application are now believed to be in condition for allowance. Favorable consideration and a Notice of Allowance are earnestly solicited.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Respectfully submitted,
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